

PATENT SPECIFICATION

(11) 1 574 302

1 574 302

(21) Application No. 24070/78 (22) Filed 30 May 1978 (19)
(31) Convention Application No. 809961 (32) Filed 27 Jun. 1977 in
(33) United States of America (US)
(44) Complete Specification Published 3 Sep. 1980
(51) INT. CL.³ A61K 47/00
(52) Index at Acceptance
ASB 823 L



(54) STABLE, SPRAYABLE ANESTHETIC SOLUTION

(71) We, SCHERICO LTD., of Topferstrasse 5, Lucerne, Switzerland, a body corporate constituted under the laws of Switzerland, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:

5 This invention relates to a stable, cosmetically elegant solution useful as a topical anesthetic when applied as a non-aerosol spray. It is relatively nonflammable and exhibits no microscopic crystallization. The preparation is designed for relief of surface pain and itching and provides soothing temporary relief of minor burns, cuts, scratches, sunburn and other minor skin irritations.

10 There are many caine-type pain relieving agents which are used in topical anesthetic compositions, the most common of which is benzocaine. Since many of these pain relieving agents are insoluble or only slightly soluble in water, solvents other than water have generally been used, such as propylene glycol as taught in U.S. Patent 2,628,182 and the polyethylene glycol esters taught in U.S. Patent 3,322,624. However, the resulting preparations were generally found to be unstable, particularly at low temperatures, with the pain-relieving agent crystallizing or settling out. The problem is particularly acute for topical anesthetic concentrations over 0.5%. This problem is especially serious in a spray device since the crystals can block the outlet orifice of the container and render the device inoperable.

15 Topical anesthetic compositions have traditionally been sold in the form of ointments, lotions, creams, and aerosol and non-aerosol sprays. The sprays are particularly desirable since they are convenient and present no danger of contamination to the product. They provide a generally desirable cooling effect on sunburned skin and cause less irritation to sensitive skin than would be produced by the rubbing on of a lotion or like product.

20 However, the aerosols containing fluorocarbon propellants are undesirable for environmental reasons and the hydrocarbon propellants are highly flammable.

25 The non-aerosol spray compositions which contain water-insoluble caine-type anesthetics generally require a high concentration of solvent to dissolve the anesthetic. Unfortunately, a system which contains more than 35-40 percent of an alcohol solvent will tend to dry the skin and is potentially hazardous since it tends to be highly flammable. If the alcohol solvent concentration is decreased to a safe level, the formulation is subject to microscopic crystallization of the anesthetic and generally gives a poor spray pattern.

30 A stable, relatively nonflammable, cosmetically elegant, sprayable topical anesthetic formulation has now surprisingly been found. This formulation is an aqueous solution containing 0.2 - 2.5 percent of a water-insoluble topical caine-type anesthetic, such as benzocaine; 0.3 - 0.6 percent of di-(C₅-C₈) alkyl sodium sulfosuccinate; 20 - 35 percent of a cosmetically acceptable, water-miscible alcohol in which the caine-type anesthetic is soluble; 10 - 25 percent of a cosmetically acceptable, water-miscible glycol which is a liquid at 25°C and in which the cain-type anesthetic is soluble; the maximum concentration of said solvents being 47 percent; and at least 50 percent water. The resulting formulation is stable at low temperatures, does not excessively dry the skin, exhibits a good spray pattern, and does not exhibit the high flammability characteristically associated with high concentrations of flammable solvents.

35 The formulation can be used in any non-aerosol spray assembly. Many such spray assemblies are widely known and used, such as the squeeze spray assembly shown in U.S.

40

45

Patents 3,361,304 and 3,474,936, or the pump spray system shown in U.S. Patents 4,010,874 and 4,022,354. The spray assembly will generally comprise a reservoir for holding the sprayable composition; a means for mixing the composition with air; and a means to dispense the air/liquid mixture as a spray. This is usually accomplished by creating a pressure differential between the atmosphere and the inside of the container, e.g. a pumper or squeezing a resilient container wall.

For purposes of this specification, the term "caine-type" anesthetic is used to refer to those amino-substituted phenyl esters and amides distinguishable by having a generic name ending in the syllable "caine". (See U.S. Patent 3,624,224.) Benzocaine is the most common compound in this class to be used in topical anesthetic formulations. Other suitable water-insoluble caine-type anesthetics are lido-caine, dibucaine and tetracaine. At least 1 percent anesthetic is preferred in this product with the most preferred range being 1 - 2 percent.

There are several suitable di-(C₅-C₈) alkyl esters of sodium sulfosuccinate which are commercially available, such as dioctyl sodium sulfosuccinate, dihexyl sodium sulfosuccinate, and diamyl sodium sulfosuccinate. The preferred compound is dioctyl sodium sulfosuccinate in a concentration of 0.4 - 0.5 percent.

Suitable water-miscible alcohol solvents are isopropyl alcohol and ethyl alcohol. Suitable water-miscible glycol solvents are propylene glycol and polyethylene glycol having a molecular weight of 200 - 600. A preferred composition contains 35 - 45 percent of solvents and most preferably contains 20 - 25 percent of isopropyl alcohol and 15 - 20 percent of polyethylene glycol having a molecular weight of 200 - 600. When reference is made to the solubility of the anesthetic in either of the solvents, a solubility of at least 5 percent in the solvent at 25°C is meant.

The concentration of water is at least 50 percent with a preferred concentration of 50 - 60 percent.

Various optional ingredients may be included in the formulation such as perfumes; preservatives, e.g. parabens; antiseptics, e.g. triclosan, phenol; humectants; emollients; antioxidants; chelating agents, e.g. disodium EDTA; dyes; foaming agents; as well as any other class of material whose presence may be cosmetically or otherwise desirable. Phenol, which is primarily used for its antiseptic properties, has also surprisingly been found to improve the low temperature stability of these formulations in concentrations of 0.2 - 0.5 percent.

The following non-limiting example is presented to illustrate the invention. The terminology is in conformance to the CTFA Cosmetics Ingredient Dictionary, 1977 edition. The percentages used throughout the specification and the claims are weight percents unless indicated otherwise.

Example

40 A topical anesthetic solution is prepared according to the following formulation:

	Part A	Weight (kg)	
45	Water	55.65	
	Isopropyl Alcohol	13.75	45
	Disodium EDTA	0.05	
	Dioctyl Sodium Sulfosuccinate	0.45	
Part B			50
50	Isopropyl Alcohol	11.25	
	Polyethylene Glycol (M.W. 400)	16.40	
	Triclosan	0.10	
	Benzocaine	2.00	
55	Phenol 90% Solution	0.35	55
		<u>100.00 kg</u>	

60 The ingredients of Part A are agitated until all solids dissolve. The ingredients of Part B are agitated until a solution results. The mixture of Part B is then blended with the mixture of Part A. The pH of the resulting formulation is 6.5.

WHAT WE CLAIM IS:-

1. A stable sprayable anesthetic solution comprising:
0.2 - 2.5 percent of a water-insoluble caine-type anesthetic;
0.3 - 0.6 percent of a di-(C₅-C₈) alkyl sodium sulfosuccinate;

5

10

15

20

25

30

35

40

45

50

55

60

65

20 - 35 percent of a water-miscible cosmetically acceptable alcohol solvent in which said anesthetic is soluble;

10 - 25 percent of a water-miscible cosmetically acceptable glycol solvent which is a liquid at 25°C and in which said anesthetic is soluble; and

5 at least 50 percent water,
wherein the maximum concentration of said solvents is 47 percent.

2. A composition according to claim 1 wherein the concentration of the caine-type anesthetic is 1 to 2 percent.

3. A composition according to claim 1 or 2 in which said caine-type anesthetic is benzocaine.

10 4. A composition according to any one of claims 1 to 3 wherein the total concentration of the solvents is 35 - 45 percent.

5. A composition according to any one of claims 1 to 4 which, as the alcohol solvent, comprises 20 - 25 percent of isopropyl alcohol and, as the glycol solvent, 15 - 20 percent of polyethylene glycol having a molecular weight of 200 - 600.

15 6. A composition according to any one of claims 1 to 5 wherein said sulfosuccinate is dioctyl sodium sulfosuccinate.

7. A composition according to claim 6 wherein the dioctyl sodium sulfosuccinate concentration is 0.4 to 0.5 percent.

20 8. A composition according to any one of claims 1 to 7 in which said water concentration is 50 - 60 percent.

9. A composition according to any one of claims 1 to 8 further comprising 0.2 - 0.5 percent phenol.

25 10. A topical analgesic product comprising:
a non-aerosol spray assembly; and
a composition as claimed in any one of claims 1 to 9 within said assembly.

11. An anesthetic composition according to claim 1 and substantially as hereinbefore described.

30 12. A topical analgesic product according to claim 10 and substantially as hereinbefore defined.

35

MATHYS & SQUIRE
Chartered Patent Agents
10 Fleet Street,
London E.C.4.
Agents for the Applicants.

35